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THE SIGNIFICANCE OF FEVER IN INFANTS LESS THAN THREE MONTHS OLD. A RETROSPECTIVE REVIEW OF ONE YEAR'S EXPERIENCE AT BOSTON CITY HOSPITAL'S PEDIATRIC WALK-IN CLINIC

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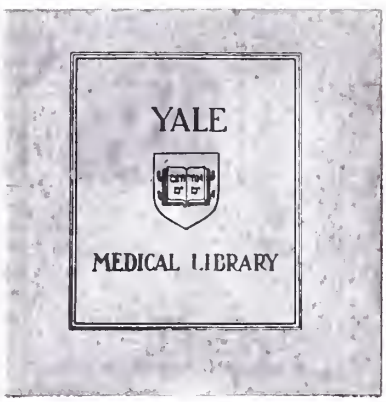
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May 20, 1982

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A THESIS SUBMITTED TO THE YALE UNIVERSITY SCHOOL OF MEDICINE IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF DOCTOR OF MEDICINE

1982

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ACKNOWLEDGMENTS

I would like to thank the staff of the Medical Records Department of Boston City Hospital, especially Harriet McDonald and Celia Wcislow for assitance in obtaining patient records. I would also like to thank Suzette Morelock who did the computer programming.

I would like to thank Jerome Klein, M.D. for sponsoring this project. Steven Pelton, M.D., Robert Baltimore, M.D., and Howard Pearson M.D. also provided valuable suggestions during completion of this project and reviewed the final manuscript. I would especially like to thank Raymond Karasic M.D. for advice and assistance throughut the completion of this project.

ABSTRACT

The hospital records of all outpatient infants 92 days of age or less with rectal temperature ≥ 100 °F and/or chief complaint of fever who presented to Boston City Hospital's Pediatric Walk-In Clinic (PWIC) in the year 1981 were reviewed. There were 187 total study visits. The rectal temperature (T) in the PWIC was ≥ 100 °F in 132 visits; half of these visits (66) were for T ≥ 101 °F. The number of patients presenting with T ≥ 101 °F increased with each month of age. The majority of study visits (56.1%) were for mild, self-limited illnesses; 14.4% of all visits were for serious illnesses (pneumonia, meningitis, bacteremia, urinary tract infection, and septic arthritis/osteomyelitis). The percentage of patients with serious illness was significantly greater in those visits for T ≥ 101 °F (31.8%) versus those for T < 101 °F (4.2%). Age less than one month was a risk factor for serious illness in febrile infants (T ≥ 100 °F in the PWIC): 30.4% of febrile infants ≤ 30 days old had serious illness versus 14.7% of febrile infants 31-92 days old. Serious illness was significantly more prevalent when the WBC count was ≥ 10,000/mm^3, percent PMNs was ≥ 50 , or absolute PMNs was ≥ 5000/mm^3. Of these parameters, WBC ≥ 10,000/mm^3 was the most sensitive (85.7%) indicator of serious illness. In this study, 42.2% of patients ≤ 30 days old with T > 100 °F and WBC ≥ 10000/mm^3 or 31-92 days old with T ≥ 101 °F and WBC ≥ 10,000/mm^3 had serious illness; therefore a full evaluation for sepsis should be considered in any infant fulfilling these screening criteria.

INTRODUCTION

The young infant less than 3 months of age presenting with fever often represents a diagnostic and therapeutic dilemma for the practicing physician. On the one hand, it is well established that infants in this age group are at higher risk for life threatening infection than older children (1-3). On the other hand, there is evidence that the majority of outpatient febrile young infants do not have serious infections (4-7). The problem for the clinician is to distinguish between the few febrile infants who are seriously infected and the many with self-limited illnesses. This is not an easy task, as significant infection in this age group is often characterized by non-specific signs and symptoms.

In an 8 month prospective study at Johns Hopkins (8) designed to determine the accuracy of clinical judgment in assessing febrile (rectal temperature $\geq$ 38°C) outpatient neonates 8 weeks of age or less, one of nine infants with bacteremia was felt to be clinically well. This infant might have been sent home with no treatment if there had not been a protocol requiring full evaluation for sepsis and intravenous antibiotic therapy for all febrile infants in this age group. Citing this study, some have argued that strict management protocols are necessary. Others have argued that the incidence of bacteremia at Johns Hopkins appears to be unusually high, and that in institutions with a lower incidence of bacteremia, no ill effects have resulted

from using a more selective approach to managing these infants (4-6).

Greene and his coworkers (4) conducted a survey to determine how febrile (rectal temperature $\geq$ 100° F) infants less than 2 months old are actually managed. These authors sent questionaires to pediatric practitioners and chief residents in pediatric training programs. They found that although in over 2/3 of the university programs chest x-ray, urinalysis, and lumbar puncture are routine for all such infants, usage of such diagnostic tests is more selective by practitioners. Less than 1/5 of the practitioners routinely perform lumbar puncture. The majority of practitioners admit less than 10% of all such patients while the majority of the university programs admit "essentially all" such patients.

Thus, it is clear that the approach to young febrile infants is entirely non-uniform. This is a result of the lack of clear guidelines in the literature. Although McCarthy and Dolan (7) have identified high fever (rectal temperature $\geq$ 104° F) as a risk factor for serious infection in infants less than 3 months old, no other studies have defined other factors which increase the risk for these patients. The purpose of this study is to determine the prevalence of serious illness and the risk factors (demographic, historical, clinical, and laboratory) which increase the likelihood of serious illness in febrile young infants. This is a first step in the attempt to provide a more rational basis for managing this difficult clinical problem.

MATERIALS AND METHODS

The Pediatric Walk-In Clinic (PWIC) of Boston City Hospital (BCH) serves its inner city patient population both as an emergency room and as a "walk-in" clinic for routine complaints. Nearly all patients who are admitted to the pediatric service pass through the PWIC. For this study, the PWIC log sheets for the year 1981 were reviewed. The names of all infants 92 days of age or less were recorded, and their charts were screened. The charts of all those patients with fever (rectal temperature in the PWIC 100°F or greater) or chief complaint of fever (including those without documented fever in the PWIC) were selected for detailed review.

A record form (Figure 1) was completed for each study visit. Information obtained from the hospital record included age, sex, racial/ethnic origin, date of visit, chief complaint, predominant symptoms at presentation, and temperature at home and in the PWIC. If specifically noted on the chart, the house officer's impression of the patient's mental status (alertness, irritability, consolability) and overall "toxicity" were recorded. In recording such subjective data, no attempt was made to interpret the information on the patient's record. The existence of illness in family members, potential risk factors for infection (such as a ventriculoperitoneal shunt), prior antimicrobial therapy (within three days of the visit), and prior antipyretic therapy (within four hours of the visit) were noted. If ordered, the white blood cell (WBC) count and differential, platelet count,

erythrocyte sedimentation rate (Westergren method), urinalysis, chest x-ray, spinal fluid analysis, and any culture results were recorded. The initial PWIC diagnosis was recorded as written by the house officer on the PWIC record. The final diagnosis was assigned retrospectively by the investigator, taking into account additional data, including culture results and official readings on chest x-rays, not available to the house officer at the initial visit.

The final diagnosis of meningitis was assigned whenever there were more than 10 WBCs/mm^3 in the spinal fluid. A final diagnosis of pneumonia required a radiographic infiltrate. The criteria for a final diagnosis of urinary tract infection were either a single organism with a colony count of greater than 10^5 from a bag specimen or a positive bladder tap. The diagnosis of septic arthritis or osteomyelitis required a positive bone or joint culture or a positive bone or joint radiograph, with or without a positive blood culture. Cultures from any source which grew Staphylococcus epidermidis or diphtheroids were considered to be contaminated and were not included as positive.

The diagnosis of otitis media was made clinically using pneumatic otoscopy. At BCH, most infants less than three months old with an initial diagnosis of otitis media are admitted. In the year of the study, it happened that all such patients were admitted. This means that the PWIC physician's clinical diagnosis of otitis media was confirmed on at least two other examinations by other resident physicians for every patient visit with a final diagnosis of otitis media.

For purposes of analysis, final diagnoses were assigned to one of 3 categories representing varying severity of illness (Table 1). Group 1 included illnesses which are generally mild and self-limited: upper respiratory infection (URI), fever no source, well baby, mastitis, skin/wound infection, conjunctivitis, and a group of miscellaneous mild ailments such as constipation and diaper rash listed as "other". The diagnosis of gastroenteritis, otitis media, bronchiolitis, croup, and varicella were assigned to Group 2, representing illnesses with a more variable course. Group 3, the category for serious illness, consisted of pneumonia, meningitis, bacteremia, septic arthritis/osteomyelitis, and urinary tract infection (UTI).

Whenever there were two diagnoses, the most serious diagnosis was considered the final diagnosis. If the two diagnoses were of equal severity, the diagnosis which appeared to be most responsible for the patients clinical presentation was chosen as the final diagnosis.

Based on the final diagnosis and the laboratory information for each study visit, a microbiologic diagnosis of proven bacterial, probable bacterial, proven viral, probable viral, other infectious, non-infectious, or unknown was assigned. A culture which grew a recognized bacterial pathogen from the appropriate body fluid was necessary for the diagnosis of proven bacterial disease. The diagnosis of proven viral disease required positive culture, serology, histology, or other specific diagnostic test. The diagnosis of probable bacterial and probable viral were assigned based on the most likely pathogen in cases

where no proof was available. For example, all otitis media was considered to be probable bacterial. All culture-negative meningitis was considered to be probable viral. All gastroenteritis was considered probable viral unless a bacterial pathogen was isolated from the stool. When insufficient information was available to make a proven bacterial or proven viral diagnosis in a patient with pneumonia, the microbiologic diagnosis was assigned on the basis of the chest x-ray. A segmental consolidation was considered to be probable bacterial whereas a patchy bronchopneumonia was considered probable viral. If positive chlamydia cultures or serology were obtained on a patient with pneumonia, the diagnosis was considered other infectious (even though chlamydiae are bacteria) because of the atypical nature of the infectious illness that they cause. For similar reasons, mycobacterial infections were considered other infectious. Parasitic and fungal infections were also included in this category.

Finally, the disposition (home or hospital), initial antimicrobial therapy, and the outcome (complicated or uncomplicated) were recorded. All data were codified and entered into a computer, and analyzed to identify relationships among variables. The statistical tests employed included chi-square, Student's t-test, Fisher's exact test, and simple linear regression.

As a check on the data-gathering methods, the BCH Bacteriology Laboratory's log of positive blood cultures was reviewed, and all patients 3 months of age of less with positive blood cultures from the PWIC during 1981 were identified. One of the patients identified had not been included in the study because she was

afebrile on presentation; this case will be discussed in the Results sction.

RESULTS

The PWIC log sheets recorded 26,653 visits of children ages infancy-18 years in 1981. There were 984 visits of infants 92 days of age or less. Records for 34 out of the 984 visits of infants ≤ 92 days were not obtainable or no temperature was recorded. The diagnoses recorded in the log sheets in most of these 34 cases suggested mild ailments (e.g. constipation, umbilical granuloma) not generally associated with fever. The detailed review comprised 189 visits by 169 patients. (20 of the visits were by patients who had previously been seen in the PWIC.) Two of the 189 study visits were by patients who had received their initial work up at other hospitals and were transferred to BCH because of complications. These two visits were excluded from analysis.

Demographic Data

The distribution of patient-visits by age is shown in Table 2. The number of study visits increased with each 15-day increment in age. Eighty-two or 43.9% of study visits were by males and 104 or 55.6% were by females. (One patient's sex was not specified.) There were 20 visits by white patients (10.7%), 113 by black patients (60.4%), 53 by Hispanic patients (28.3%), and 1 visit by a Native American (0.5%).

Distribution of Temperature in the PWIC

No rectal temperature was recorded in the PWIC for two of the study visits. The rectal temperature (T) in the PWIC was

$\geq 100^{\circ}$F in 132 of the remaining 185 visits (71.4%). Half of these patients (66) had a T $\geq 101^{\circ}$F. Thus the overall prevalence of fever $\geq 101^{\circ}$F in patients $\leq$ 3 months presenting to the PWIC is 66/984 = 6.7%.

Figure 2 shows the distribution of patient visits by temperature and by age. There were no significant age differences in the proportion of patients presenting with T $\geq 101^{\circ}$F; however, the absolute number of patients with this degree of fever increased with each month of age. The two patients with high fever (T $\geq$ 104) were both over 75 days old.

Disposition

Overall, 37.3% of study visits resulted in admission to the hospital. Of febrile infants (T $\geq 100^{\circ}$F), 48.5% were admitted, and the percentage increased with increasing temperature. Of febrile infants $<$1 month, 78.3% were admitted.

Of those patients initially sent home, the majority (57.0%) recovered uneventfully. No follow up was obtained on 35.3%. A small percentage (7.0%) returned to the PWIC during the same course of illness and were admitted. Of those initially admitted to the hospital, 93.8% recovered uneventfully, while 4 patients (6.2%) had a complication (febrile seizure (1), apnea spell (1), and readmission within two weeks for septic arthritis/osteomyelitis (2)). There were no deaths.

Distribution of Final Diagnoses

Table 3 shows the distibution of final diagnoses for all study patients. The most prevalent diagnosis was URI (21.4%), with

fever no source, otitis media, gastroenteritis, pneumonia, and well baby being the next most common diagnoses, each accounting for 7 - 13% of the total. The prevalence of otitis media was actually greater than depicted on Table 3 because otitis was a frequent second diagnosis. Of the 9 study visits with two diagnoses, 8 had otitis as the second diagnosis. (The 9th visit was for gastroenteritis and bronchopneumonia). Of the 14 visits for pneumonia, 3 were proven viral (see below), 1 was chlamydial, 5 were classified as probable viral and 5 as probable bacterial. Salmonella was cultured from the stool in 4 of the 20 visits for gastroenteritis; the rest were classified as probable viral. Three of the 4 visits with a final diagnosis of Salmonella gastroenteritis were by one patient during his two month course of illness.

Of the 5 visits for meningitis, all were culture-negative (probable viral). Three of these patients had a cerebrospinal fluid (CSF) pleocytosis of $\geq$ 300 white blood cells (WBC)/ mm^3; all three cases occurred in late June or July. In the other two patients, there was a lesser pleocytosis of 12 - 13 WBC/ mm^3 with 2-3 polymorphonuclear neutrophils (PMNs)/mm^3 in the differential. Both of these patients had concurrent otitis media. One of the visits was in March and the other was in July.

The organism in the blood of all three bacteremic patients was Group B Streptococcus. Group B Streptococcus was also isolated from the joint fluid but not the blood of one of the two patients with septic arthritis/osteomyelitis. The second

patient with osteomyelitis was diagnosed based on radiographic and radionuclide evidence; no cultures were positive. Escherichia coli was the etiologic agent in all three patients with urinary tract infection.

Table 3 gives the 21 diagnoses that were classified as "other". One patient who presented with a high fever (104°F) had no urinalysis performed during her original evaluation. A spinal tap, chest x-ray, and blood and CSF cultures were negative. Mixed flora grew from a bag urine specimen. Subsequent bladder taps and urinalyses, all performed after intravenous antibiotic therapy had been given, were negative. The final diagnosis, possible urinary tract infection, was classified as "other" and the microbiologic diagnosis of "unknown" was assigned.

Table 1 gives the distribution of final diagnoses among the three categories of severity. The majority of study visits (56.1%) were for mild, self-limited illnesses. Only 14.4% of all visits were for Group 3 (Serious) illness. The remaining 29.4% were for Group 2 illnesses (Variable Severity)

Distribution of Microbiologic Diagnoses

Table 4 shows the distribution of microbiologic diagnoses. The majority of illnesses (56.1%) were of probable viral origin. Only 6.6% were of proven bacterial origin. The diagnoses that were included in the categories of proven bacterial, proven viral, other infectious, and unknown, are included on the table. (All cases of proven viral disease were cases where nasopharyngeal secretions were positive for respiratory syncytial

virus antigen by an immunofluorescence technique performed at the Virology Laboratory of Children's Hospital Medical Center, Boston.

Relationship of Final and Microbiologic Diagnoses to Temperature

Table 5 gives the distribution of final diagnoses among three temperature ranges ($T \leq 100^{\circ}F$; $T = 100.0\text{-}100.9^{\circ}F$; and $T \geq 101^{\circ}F$). Of those with $T \geq 101^{\circ}F$, 31.8% had serious illness, while only 3-5% of those with lower temperatures had serious illness. Approximately 40% of patients with $T \geq 101^{\circ}F$ had Group 1 illness. The proportion of Group 1 illness increased significantly as temperature decreased. Approximately 80% of patients with $T \leq 100^{\circ}F$ had Group 1 illness. Group 2 illness was more than twice as prevalent in patients with $T \geq 100^{\circ}F$ than in the afebrile group (34.1% versus 15.1%). These relationships are also depicted on Figure 4.

Table 6 shows that the proportion of bacterial (proven plus probable) illness increased with increasing temperature, from 7.5% at $T \leq 99.8^{\circ}F$ to more than 50% at $T \geq 102^{\circ}F$. This trend achieved statistical significance when those with $T < 101^{\circ}F$ were compared to those with $T \geq 101^{\circ}F$ ($X^2 = 34.6$; $p < 0.001$). The proportion of viral illness (proven plus probable) remained relatively constant at 55-70%. (At the highest temperatures, the percentage dropped, but the numbers are low and this is not statistically significant.) These relationships are depicted graphically in Figure 5. (Note that the one patient with a microbiologic diagnosis of unknown is not included on this figure; therefore the percentages do not equal 100 at $T = 104.0\text{-}104.9^{\circ}F$.

Demographic Risk Factors

As infants with T < 100°F infrequently had serious disease, most of the subsequent analysis concerns patients who were febrile (T ≥ 100°F) in the PWIC. The distribution of final diagnoses in febrile infants by age in months is shown in Table 7. The proportion of Group 3 illness in infants ≤ 30 days old (30.4%) was significantly greater than in 31-92 day olds (14.7%) (X^2 = 4.26; p < 0.05). Both cases of septic arthritis/osteomyelitis were in infants less than one month old, as were 2 of the 3 cases of bacteremia. The proportion of Group 1 illness remained relatively constant with age at 40-55%. The prevalence of Group 2 illness was significantly lower in the first month of life (17.4%) than in the next two months (39.4%) (p = 0.025; Fisher's exact test). Figure 6 depicts these relationships graphically. The same age-related trends were evident if only infants with T≥ 101°F were considered, but the numbers were low and statistical significance was lost. A striking finding was that all 4 infants 5-15 days old with T ≥ 101°F had Group 3 illness.

In Table 8, some relationships of microbiologic diagnosis to age in febrile infants are demonstrated. Bacterial (proven plus probable) illness was significantly more prevalent in the first month of life (43.5%) than in the second (18.4%). Proven bacterial illness was also significantly more common in the first than in the second and third months (17,4% versus 5.5%) (p = 0.0013; Fisher's exact test. Three of the 4 cases of proven Group B Streptococcal disease occurred in infants less than 1 month old. There were no significant differences in the prevalence

of viral disease among the three age groups.

There were no significant differences in the distribution of final or microbiologic diagnoses among febrile infants grouped by sex or by racial/ethnic origin.

Historical Risk Factors

Sixty-three patients (33.7%) of study patients had had a rectal temperature taken at home before coming to the PWIC. As shown in Figure 3, if there was a discrepancy between the two, the temperature at home was almost always higher. There was a significant correlation between the two ($R = 0.46$; $p = 0.0001$).

Twelve patients had received antipyretic therapy (aspirin or acetaminophen) within four hours of their visit. The mean temperature in this group was 101.2 +/- 1.4°F versus a mean temperature of 99.7 +/- 1.0°F in the 14 patients who were specified as receiving no antipyresis. Only two patients who had been given antipyretics were afebrile on presentation.

The distribution of chief complaints among all study patients is shown in Table 9. Fever was the most common chief complaint, accounting for 35.8% of the total. Fever and respiratory symptoms (15.0%) and respiratory symptoms (11.2%) were next in prevalence. Systemic symptoms (anorexia, sleep disturbance, or irritability) were infrequent (3.2%) chief complaints.

Among predominant symptoms at presentation, shown in Table 10, respiratory symptoms were most prevalent (34.2%), followed by gastrointestinal (13.9%) and systemic (13.4%) symptoms. In Table 11, the distribution of predominant symptoms

in febrile versus afebrile patients is shown. The proportion of patients with systemic symptoms (alone or in combination with other symproms) was significantly greater in febrile patients (X^2 = 11.8; $p < 0.001$). However, among febrile patients, there was no difference in the incidence of serious illness between patients with systemic symptoms and those without them.

The presence or absence of potentially infectious illness in family members was specified in 102 or 55% of patients. In 46 patients or 45% of those specified, there was no illness in family members. Among the remaining 56 patients, the illness in family members was respiratory in 45, gastrointestinal in 3, and other in 8. There was no difference in the prevalence of serious illness between those with (16.1%) and those without (19.6%) illness in family members. The distribution of microbiologic diagnoses were similar in the two groups as well.

The distribution of perinatal complications is shown in Table 12. For most patients (94.7%), perinatal history was specified. 28 or 14.9% of patients had a history of prematurity (less than 37 weeks gestation), low birth weight (less than 2500 grams), prolonged rupture of membranes (greater than 24 hours), and/or maternal fever at the time of delivery. In Table 13, the relationship of a history of these complications in patients presenting to the PWIC with fever ($T \geq 100°F$) to seriousness of final diagnosis is shown. The prevalence of Group 2 plus Group 3 illness was significantly greater in patients with perinatal complications (68.8%) versus those without complications (46.2%) ($p = 0.004$; Fisher's exact test). There were no differences in the distribution of microbiologic

diagnoses between these two groups.

There were 18 visits of infants who were considered to have potential risk factors for infection. Any infant who had previously had a serious infectious illness or who had had a minor infectious illness within 2 weeks of the visit was considered potentially at higher risk. There were 14 such visits. In addition, there were 4 patient-visits in which special pathologic or iatrogenic conditions which predisposed to infection were present (ventriculoperitoneal shunt, gastroesophogeal reflux, recent pyloromyotomy, and recent intravenous line placement). Three patient-visits for which the past medical history was not specified were excluded from analysis. There were no significant differences in the proportion of serious illness or in the distribution of microbiologic diagnoses among febrile infants with and without potential risk factors.

Two patients had been receiving antibiotic therapy (amoxicillin in both cases) within three days of thir visit. As the number was low, no further analysis was performed.

Physical Examination Risk Factors

No patients were described as being "toxic". Consolability was specified in 49 patients; two patients were described as not consolable. Both of these patients had a final diagnosis of fever no source. This data was not analyzed further because of the low numbers.

In 77.0% of patients mental status was specified. Of those specified, 92 or 63.4% were described as alert, 46 or 31.7% were described as irritable, 2 or 1.1% were described

as lethargic, and 4 or 2.1% were described as irritable and lethargic. For purposes of analysis, irritability and/or lethargy were considered togetner as "altered mental status". There was a significant increase in the proportion of patients with altered mental status with increasing temperature. In order to control for the effect of temperature, the relationship of altered mental status to final diagnosis was analyzed at three temperature ranges ($100 \leq T < 101\,^{\circ}F$, $101 \leq T < 102\,^{\circ}F$, $T \geq 102\,^{\circ}F$). The results are shown in Table 14. For patients with $101 \leq T < 102\,^{\circ}F$ there was a significantly greater proportion of Group 2 and 3 illness (85.6%)in patients described as irritable and/or lethargic than in patients described as alert (41.1%).

Laboratory Risk Factors

Use of diagnostic tests is selective at BCH. Blood cultures were obtained in 96 (51.3%) visits, urine analyses in 82 (43.9%), chest x-rays in 103(56.6%), spinal fluid analyses in 56 (29.9%), and complete blood counts in 100 (53.5%). The higher the patient's temperature, the more likely these diagnostic tests were performed.

Table 15 gives the distribution of final diagnoses in febrile patients by WBC count. Group 3 illness occurred over the full range of WBC count but was significantly more common when WBC $\geq 10{,}000/mm^3$ ($p = 0.006$; Fisher's exact test). Group 1 illness was significantly more common in infants with WBC $< 10{,}000/mm^3$ ($\chi^2 = 5.02$, $p < 0.05$). However, Table 16 shows that there were no statistically significant differences in the

prevalence of bacterial or viral disease with varying WBC count in febrile patients.

The relationship of percent PMNs to final and microbiologic diagnoses in febrile infants are shown in Tables 17 and 18. Serious disease was significantly more prevalent when percent PMNs $\geq$ 50. (X^2 = 5.01, $p < 0.05$). The proportion of proven plus probable bacterial illness was significantly higher when the percent PMNs was greater than 25 (X^2 = 6.53; $p < 0.05$). Viral illness was more common when the percentage of PMNs was <50 (X^2 = 8.14, $p < 0.01$).

Tables 19 and 20 give final and microbiologic diagnosis versus absolute PMNs in febrile infants. Group 3 illness was significantly more prevalent when absolute PMNs were $\geq$ 5000/mm^3 (X^2 = 6.84, $p < 0.01$). Viral illness was significantly more common with absolute PMNs $<$ 5000/mm^3 (X^2 = 5.21; p 0.05), while bacterial illness was significantly more common with absolute PMNs $\geq$5000/mm^3 (X^2 = 6.85, $p < 0.01$).

No relationship between percent bands and seriousness of diagnosis was demonstrated by the data (Table 21). However, proven bacterial illness was more common when the percentage of bands was greater than 5, while proven plus probable viral illness was more prevalent when percent bands was 5 or less (Table 22).

Finally, the data for absolute band counts are presented in Tables 23 and 24. Group 3 illness was more common in those with a band count of $\geq$1500/mm^3 versus those with a count less than 250/mm^3 (p = 0.04; Fisher's exact test). Proven plus probable

bacterial illness was significantly more common when the absolute band count was $\geq 250/mm^3$ ($X^2 = 7.91$; $p < 0.01$), while proven plus probable viral illness was significantly more common when the band count was $< 250/mm^3$ ($X^2 = 5.12$, p 0.05).

The sensitivity and specificity (as defined by Feinstein (9)) of the various WBC parameters for serious illnes are summarized in Table 25. The relationship of combined age, temperature, and WBC criteria to seriousness of illness is shown in Tables 26 and 27.

An erythrocye sedimentation rate was obtained on only 5 patient-visits. Therefore it was not included in any further analysis.

Review of Positive Blood Cultures

The review of positive blood cultures from 1981 revealed that no febrile bacteremic outpatient infants less than three months old had inadvertantly been left out of the study. However, one 4 week old infant who presented with a respiratory rate of 113/minute and a temperature of 99.0°F and who was admitted for bilateral pneumonia on chest x-ray, had *E. coli* isolated from her blood (trypticase soy broth medium) after 18 hours incubation. Repeat blood cultures (after intravenous ampicillin and gentamycin therapy had been initiated) were negative. The patient was treated for 10 days with intravenous antibiotics and recovered uneventfully.

DISCUSSION

The results show that fever is an uncommon occurrence in infants less than three months old presenting to an urban emergency room . When it does occur, the majority of patients have mild, self-limited illnesses. The data demonstrate several factors which increase the likelihood that a febrile infant will have serious illness: age one month or less, temperature $\geq$ 101 F, WBC count greater than 10,000/mm^3, percent PMNs $\geq$ 50, and absolute PMNs $\geq$ 5000/mm^3. In the discussion below, each of these points will be considered in turn. Following this, the implications of these findings for patient management will be discussed.

The prevalence of fever $\geq$ 101 °F in infants less than three months old presenting to the PWIC (6.2%) is not unexpectedly higher than that reported by Pantell (1.4%) for a family practice clinic (6) and that reported by Hoekelman et al. (1.3%) for private pediatric practice (10). Unfortuneately, comparable prevalence data are not available for other urban emergency rooms. Some comparisons can be made, however. The number of infants less than three months presenting with fever $\geq$ 100°F in a 15-month period to the Yale-New Haven Hospital was 149 (7), an average of 9.9 visits/month, while the average number of visits/month to the PWIC of infants with this degree of fever was 11.0. At Johns Hopkins, there were 61 visits of infants 8 weeks or less with fever $\geq$ 100.4 °F over an 8-month period, or 7.6 visits/month (8). (Infants afebrile on presentation but with documented fever > 100.4 °F at home were included.) The comparable figure at

BCH (which does not, however, include any infants who were afebrile on presentation) was 3.8 visits/month. At an inner city community hospital in Nashville, there were 37 visits of infants less than 2 months with fever $\geq$ 100°F over a 6 month period, or 6.1 visits/month (4). The comparable figure at BCH is 6.0 visits/month.

Data from other institutions also support the finding at BCH that most infants in this age group with fever $\geq$ 100°F have mild, self-limited illnesses. In the Yale study mentioned previously (7), the prevalence of serious disease (defined as sepsis, pneumonia, bacterial meningitis, and severe gastroenteritis with dehydration) in patients with $100 \leq T < 104$°F was 9.5%, while the comparable figure using the BCH data (excluding the cases of aseptic meningitis from the "serious" category) is 13.1%. At an inner city community hospital in Nashville, there was a 5.4% prevalence of serious illness (as defined in the present study) in infants $<$ 2 months with fever $>$ 100°F; the figure at BCH for for patients this age with this degree of fever was 16.7%. In the Hopkins study (8), bacteremia, meningitis, and pneumonia occurred in 32.8% of patients eight weeks of age or less with fever $\geq$ 100.4°F; at BCH, 26.7% of patients in this age and temperature category had Group 3 illness.

Although the prevalence of serious illness is similar in the BCH and Hopkins series, the relative proportions of pneumonia and bacteremia are reversed in the two institutions: at Johns Hopkins 4/61 (6.5%) of patients had the final diagnosis of pneumonia while 9/61 (14.8%) had a final diagnosis of bacteremia. For the comparable group of patient-visits at BCH, 2/45 (4.4%)

were for bacteremia and 4/45 (8.9%) were for pneumonia. Comparison to other studies suggests that the experience at Johns Hopkins was most unusual. While 6 bacteremic patients less than one month old were seen over an 8-month study period at Hopkins, in 20 months at Yale, there were only 3 outpatients one month of age or less with bacteremia (11). In 6 months at an inner city community hospital in Nashville, of 36 outpatient infants with fever $> 100°F$ and age $\leq$ 8 weeks, none were bacteremic (4). In a previous study at BCH (12), of all patients less than 6 months old with $T \geq 101$ presenting over a 3 month period, only one was bacteremic. In the Johns Hopkins study blood cultures were performed on all infants, while in these other studies, not every infant had a blood culture performed; therefore it is possible some bacteremic infants were missed. However, in Teele et al.'s 18-month prospective study at BCH, all infants with $T \geq 101°F$ had a blood culture performed; only 2/116 patients $<$ 6 months old were bacteremic (13).

Part of the explanation for the apparently high prevalence of bacteremia at Johns Hopkins may be related to a skew in the patient population there. Of the Hopkins study patients, 36/61 (59%) were less than one month old, while 15/45 or 33% of patients in a comparable age and temperature category at BCH were less than 1 month old. It is well established that infants less than 1 month old are at higher risk for bacteremia than older infants(14); therefore the Hopkins study population would be expected to have a higher prevalence of bacteremia than the BCH population.

In contrast to the experience at Hopkins, the data presented here show that the number of infants presenting with fever was lowest in the first month of life and increased with each month of age in the study; there were nearly 3 times more infants presenting in the third month versus the first. Pantell and his coworkers found no differences in the number of visits for low degrees of fever (T = 100.0-100.9°F) among infants this age in their family practice, but over 4 years they had 3 visits of infants less than one month versus 6 visits of infants in the third month of life for fever $\geq$ 101°F (6).

One possible explanation for the rarity of fever as a presentation in the youngest age group is that these infants have had less exposure to and are less likely to contract the viral illnesses which are the usual cause of fever in pediatric practice. Group 2 consists of illnesses which are almost entirely virally related. (Only 2 of the 15 cases of gastroenteritis among febrile infants were proven bacterial. Otitis media, while most commonly a bacterial disease, is frequently preceded by an upper respiratory infection.) Group 2 illness was significantly less prevalent in the youngest infants with fever. Although the difference does not reach statistical significance, the prevalence of proven plus probable viral illness is lower in the youngest infants (47.8% in infants 5-30 days old versus 63.3% in infants 31-92 days old). However, even if the prevalence of viral illness were the same,

if the incidence were lower, this could explain the lower incidence of fever in the youngest infants presenting to the PWIC. In Table 7, the number of visits per month of age per year for almost every virally related illness (URI, fever no source, otitis media, gastroenteritis, bronchiolitis, meningitis) is lowest in the youngest infants.

While fever presenting in the first month is rare, the data show that it is more likely to indicate serious illness than in the next two months of life. This is not surprising, as it is well documented that infants less than one month old are at greater risk for life-threatening infection than older infants (14). The organisms most often implicated in neonatal infection are Group B Streptococcus and Escherichia coli (14, 15). In this study, Group B Streptococcal disease accounted for the increased risk in very young infants. Three out of the 7 cases of serious disease in infants less than one month old were due to Group B Streptococci (2 bacteremias and 1 septic arthritis). The only other case of Group B Streptococcal illness occurred in a $2\frac{1}{2}$ month old with bacteremia. If these 4 cases are excluded from analysis, there are no longer any significant differences in the proportion of serious disease in infants of varying ages.

The degree of fever on presentation has been shown to be a risk factor for serious illness in infants less than three months old in one other study. McCarthy and Dolan (7) observed that high fever (rectal temperature $\geq 104^{\circ}F$) is associated with a high risk (36.4%) of serious illness

(sepsis, pneumonia, bacterial meningitis, and severe gastroenteritis with dehydration) in infants less than three months old. They also observed that fever of this degree was extreemly uncommon in this age group. They reviewed over 150,000 consecutive visits over more than 6 years to the Yale-New Haven Pediatric Emergency Room and found only 22 cases of fever $\geq 104^{\circ}F$ in infants less than three months old.

Excluding cases of aseptic meningitis from the "serious" category for purposes of comparison, the BCH data show that of the 66 patients with $T \geq 101^{\circ}F$, 16 or 24% had serious disease, while only 2 or 3% of the 66 patients with T = 100.0-100.9 had serious disease (p=0.0003, Fisher's exact test). The prevalence of serious illness in infants with $T \geq 101^{\circ}F$ in the BCH series (24.2%) is not strikingly different from the prevalence of serious illness in infants with $T \geq 104^{\circ}F$ in the Yale series (36.4%). It is of interest that these two sets of data suggest a trend of increasing risk with increasing temperature; however, it is perhaps more significant that the risk is relatively high even with the temperature as low as $101^{\circ}F$. The fact that a clinician will encounter approximately 30 patients with T = 101.0-103.9°F for every one with $T \geq 104^{\circ}F$ underscores the importance of this finding.

In the BCH series only two patients presented with $T \geq 104^{\circ}F$. The Yale data (7) showed that bacterial meningitis is significantly more prevalent in those young infants with temperatures $\geq 104^{\circ}F$. Perhaps the absence of cases of bacterial meningitis in the BCH series was related to the low incidence of fever of

this magnitude.

There are no other studies available which specifically compare diagnosis with height of fever in infants ≤ 3 month old. There is one closely related study, however. Pantell and his coworkers, in their review of four years experience at a family practice clinic, found 335 visits of infants less than 6 months old with temperature ≥100°F (6). They found meningitis and lower respiratory infection to be significantly more common in infants with T ≥ 101°F. Urinary tract infection occurred in 2/54 infants with T ≥ 101°F and 2/28 infants with T = 100.0-100.9 F. (This does not attain statistical significance.) Of the 54 visits for T ≥ 101°F, 12 were by patients less than 3 months old, demonstrating the rarity of fever in infants in this age group. Of the 12 patients, 1 (8.3%) had what is defined in this study as serious illness.

Although several studies have documented the diagnostic value of the WBC and differential in deep bacterial infection in children beyound the neonatal period (11-13, 16-18), it has long been assumed that the WBC count and differential are too variable during the neonatal period to be useful. In the past ten years, however, careful study has revealed that when normal ranges are delineated precisely (taking into account the infant's age in hours and days and other factors which may alter the WBC count) nearly all neonates with deep bacterial infection will fall outside the normal range on at least one of their WBC parameters. Manroe and her coworkers (19) determined "reference values" for infants 0-24 days. In obtaining these values, they not only excluded subjects with deep bacterial

infection, but those with periventicular hemorrhage, hemolytic disease, and maternal fever, as they found that these factors altered the WBC count. Their limits of normal rose from 1800-5400 total neutrophils/mm^3 at birth to 7500-14,400 at 12 hours, and then steadily declined until day 5, after which they were stable at 1800-5400/mm^3. Their maximum immature neutrophil counts and maximum immature/ toal neutrophil ratio (I:T ratio) showed a similar curve, with 500 immature forms and an I:T ratio of 0.13 being stable maximum values after day 5. These parameters had no lower limit of normal. Gregory and Hey and Xanthou found similar ranges for total neutrophils (20,21). Manroe et al. found that their normal range was quite sensitive: in none of their 156 cases of confirmed sepsis in infants $\leq$ 5 days of age were all the neutrophil factors (total neutrophils, immature neutrophils, or I:T ratio) normal. The most specific findings indicative of infection were neutropenia and an abnormal I:T ratio (52-86% specific depending on the clinical setting). Neutrophilia and an increase in immature neutrophils each had a specificity of only 50-60% depending on the clinical setting. Gregory and Hey's studies extended these findings to infants aged 4 days to 4 weeks: they found that neutrophil counts were outside their normal range (similar to Manroe's) in 27/29 (93.1%) of their infants with deep bacterial infection. Neutrophilia had a sensitivity of 79.0%. (3/14 infants with bacteremia and 1/5 infants with meningitis had neutropenia.

While the WBC data presented in Table 25 show that while previously defined guidelines for the identification of deep

bacterial infection in infants and children (WBC $\geq$ 15,000/mm^3, absolute bands $\geq$ 500/mm^3, absolute neutrophils $\geq$5000/mm^3) (11,13, 16-18) are all reasonably specific (67.5-78.4%) in this study population, they are not highly sensitive (37.8-70.0%). In attempting to screen for potentially life threatening disease where false positive results will do no great harm, a test with the greatest sensitivity is desirable. The results in Table 25 show that WBC $\geq$10,000/mm^3 and percent PMNs $\geq$ 25 are the most sensitive (86-87%) indicators of serious illness. They are also the most sensitive indicators of proven or proven plus probable bacterial illness (70-90%).

As percent PMNs $\geq$ 25 is less specific than total WBC $\geq$ 10,000/mm^3 (31.3% versus 42.2%) and as they are of comparable sensitivity, the total WBC count is a more useful diagnostic tool. Only 3 febrile patients with Group 3 illness would have been missed in this study using WBC$\geq$10,000/mm^3 as a screen (Table 15). One of these patients had pneumonia and two had aseptic meningitis. As another screening test, the chest x-ray, is avilable to aid in the diagnosis of pneumonia, and as aseptic meningitis is probably not as serious as the other diagnoses in the Group 3 category, and is in any case not specifically treatable, missing these patients is of less importance than if a potentially more occult, deep bacterial infection were missed.

Based on Table 15, the positive accuracy of WBC $\geq$ 10,000/mm^3 is 34.5%, indicating that 65.5% of patients with this value will not have serious illness (9). The positive accuracy and specificity

can be increased if age, temperature, and WBC criteria are combined. If the following two groups of patients are considered: age $\leq$ 30 days with T $\geq$ 100°F and WBC $\geq$ 10,000/mm^3 and age $>$ 30 days with T $\geq$ 101°F and WBC $\geq$ 10,000/mm^3, the positive accuracy is increased to 42.2% and the specificity is increased to 62.7% (Tables 26-27). Using these screening criteria, only 1 additional patient with Group 3 illness, a patient with pneumonia, would have been missed; however this case could have been identified by chest x-ray.

Although in this study, not every patient who satisfied the age and temperature criteria received a CBC, in a year at BCH there were only 45 patients who satisfied these age, temperature, and WBC criteria. If all these patients were admitted, this would mean at most 26 admissions a year for non-serious illness. (It is likely that some of those patients who had Group 2 illness needed to be admitted in any case.) The burden of these extra admissions is not unreasonable considering the potentially serious consequences of missing the patients with deep bacterial infection, some of whom were relatively assymptomatic and might not have been identified in any other way.

It is impossible to assess accurately the value of clinical judgment in a retrospictive study. In this study, the finding that infants with T = 101.0-101.9°F who were described as irritable and/or lethargic were less likely to have Group 1 illness than infants who were described as alert, suggests that clinicians are able to distinguish ill infants based on their behavior, at least to some degree. In their prospective study, Roberts and Borzy (8) found physician's clinical assessments

to be quite sensitive (88.9%) for bacteremia. The authors of this study concluded that clinical judgment is not infallible, however, because one bacteremic infant was felt to be clinically well. However, this 18 day old had a temperature of 101°F and a WBC count of 15,100/mm^3 with 58% PMNs and 4% bands. By the criteria outlined above, this infant should be considered at high risk for serious illness. The combined use of the screening criteria outlined above and of clinical judgment might be the optimal approach to initial management of these infants. Further prospective studies are needed.

The conclusions supported by this study are that complete evaluation for sepsis in any infant $\leq$ 30 days old with T $>$ 100°F and WBC $\geq$ 10,000/mm^3 or 31-92 days old with T $\geq$ 101°F and WBC $\geq$10,000/mm^3 will have a reasonably high yield and should be considered. In addition, infants who do not fulfill these criteria but who have respiratory symptoms are candidates for chest x-rays. Although no infants in this study were neutropenic, it is well documented that these infants are at high risk for bacteremia (19) and deserve further evaluation. It is not safe to conclude from this data that infants with negative chest x-rays and normal WBC count and/or lesser degrees of fever are free of risk, but their risk is certainly less.

Table 1. Classification of Final Diagnoses

Group 1: Mild, Self-Limited Illnesses N = 105 (56.1% of total)

Upper Respiratory Infection
Fever No Source
Well Baby
Mastitis
Skin/Wound Infection
Conjunctivitis
Other

Group 2: Illnesses of Variable Severity N = 55 (29.4% of total)

Otitis Media
Gastroenteritis
Bronchiolitis
Croup
Varicella

Group 3: Serious Illness N = 27 (14.4% of total)

Pneumonia
Meningitis
Urinary Tract Infection
Bacteremia
Septic Arthritis/Osteomyelitis

Table 2. Distribution of Patient-Visits by Age

Age (days)	Number of Patient-Visits
5-15	13
16-30	25
31-45	29
46-60	37
61-75	41
76-92	42
	187

Table 3. Distribution of Final Diagnoses

Diagnosis	Number of Patient-Visits	Percent of Total
Upper Respiratory Infection	40	21.4
Fever No Source	24	12.8
Otitis	20	10.7
Gastroenteritis	20	10.7
Pneumonia	14	7.5
Well Baby	14	7.5
Bronchiolitis	13	7.0
Meningitis	5	2.7
Bacteremia	3	1.6
Urinary Tract Infection	3	1.6
Mastitis	3	1.6
Septic Arthritis/Osteomyelitis	2	1.1
Skin/Wound Infection	1	1.1
Conjunctivitis	1	0.5
Croup	1	0.5
Varicella	1	0.5
Other *	21	11.2
	187	100.0

* Other: Oral candidiasis or candidal diaper rash (5); constipation (2); colic (2); dermatitis, various types (2); DPT reaction (2); overfeeding (1); amoxicillin-induced diarrhea (1); viral exanthem (1); minor head trauma (1); upper respiratory infection and conjunctivitis (1); anal fissure (1); status post pyloromyotomy (1); possible urinary tract infection (1)

Table 4. Distribution of Microbiologic Diagnoses

Diagnosis	Number of Patient-Visits	Percent of Total
Probable Viral	105	56.1
Probable Bacterial	30	16.0
Non-Infectious	28	15.0
Proven Bacterial*	12	6.4
Proven Viral#	5	3.2
Other Infectious**	6	2.7
Unknown##	1	0.5
	187	100.0

* "Proven Bacterial" included: Salmonella gastroenteritis (4); Group B Streptococcal bacteremia (3); E. coli urinary tract infection (3); Group B Streptococcal septic arthritis (1); Staphylococcus aureus skin infection (1)

**"Other Infectious" included: oral candidiasis (5); chlamydial pneumonia (1)

#"Proven Viral" included: respiratory syncytial virus pneumonia (3); respiratory syncytial virus bronchiolitis (2)

##"Unknown" consited of possible urinary tract infection (1) (see text)

Table 5. The Relationship of Final Diagnosis to Temperature

	Temperature (°F)					
	<100.0		100.0-100.9		101.0-104.2	
	N	%	N	%	N	%
Group 1						
URI	16	30.2	19	28.8	5	7.6
Fever No Source	5	9.4	5	7.6	14	21.2
Well Baby	10	18.9	3	4.5	2	3.0
Skin Infection	0	0	1	1.5	1	1.5
Mastitis	1	1.9	2	3.0	0	0
Conjunctivitis	0	0	0	0	1	1.5
Other	10	18.9	8	12.1	3	4.5
Total Group 1	42*	79.2	38*#	57.5	26#	39.4
Group 2						
Otitis	0	0	9	13.6	11	16.7
Gastroenteritis	5	9.4	9	13.6	4	6.1
Bronchiolitis	3	5.7	6	9.1	4	6.1
Croup	0	0	1	1.5	0	0
Varicella	0	0	1	1.5	0	0
Total Group 2	8**	15.1	26**	39.4	19	28.8
Group 3						
Pneumonia	3	5.7	1	1.5	9	13.6
Meningitis	0	0	0	0	5	7.6
Bacteremia	0	0	0	0	3	4.5
UTI	0	0	0	0	3	4.5
Septic Arthritis	0	0	1	1.5	1	1.5
Total Group 3	3	5.7	2+	3.0	21+	31.8
Total N	53		66		66	

*$X^2 = 5.37$; $p<0.05$
#$X^2 = 8.34$; $p<0.01$
+$p=0.00005$, Fisher's exact test
**$X^2 = 8.52$; $p<0.01$

Table 6. Microbiologic Diagnosis Versus Temperature

Diagnosis	Temperature (°F) ≤ 99.8 N	%	100.0-100.9 N	%	101.0-101.9 N	%	102.0-102.9 N	%
Probable Viral	28		41		22		11	
Proven Viral	1		1		3		0	
Total Viral	29	54.7	42	63.6	25	69.4	11	50.0
Probable Bacterial	2		12		6		3	
Proven Bacterial	2		2		3		8	
Total Bacterial	4	7.5	14	19.7	9	25.0	11	50.0
Other Infectious	5		1		0		0	
Non-Infectious	15		9		2		0	
Unknown	0		0		0		0	
Total Other	20	37.7	10	15.2	2	5.5	0	0
Total patients	53		66		36		22	

Diagnosis	103.0-103.9 N	%	104.0-104.2 N	%
Probable Viral	2		0	
Proven Viral	0		0	
Total Viral	2	33.3	0	0
Probable Bacterial	2		0	
Proven Bacterial	2		1	
Total Bacterial	4	66.7	1	50.0
Other Infectious	0		0	
Non-Infectious	0		0	
Unknown	0		1	
Total Other	0	0	1	50.0
Total Patients	6		2	

Table 7. The Relationship of Final Diagnosis to Age in Febrile Infants

Final Diagnosis	Age (days) 5-30 N	%	31-60 N	%	61-92 N	%
Group 1						
URI	3		14		7	
Fever No Source	4		5		10	
Well Baby	1		2		0	
Mastitis	2		0		0	
Skin/Wound Infection	1		0		1	
Conjunctivitis	0		0		1	
Other	1		5		5	
Total Group 1	12	52.1	26	53.1	24	40.0
Group 2						
Otitis Media	2		7		11	
Gastroenteritis	1		6		8	
Bronchiolitis	0		5		5	
Croup	0		0		1	
Varicella	1		0		0	
Total Group 2	4	17.4	18	36.7	25	41.7
Group 3						
Pneumonia	2		2		6	
Meningitis	1		2		2	
Bacteremia	2		0		1	
UTI	0		1		2	
Septic Arthritis/Osteo	2		0		0	
Total Group 3	7	30.4	5	10.2	11	18.3
Total N	23		49		60	

Table 8. The Relationship of Microbiologic Diagnosis to Age in Febrile Infants

	Age (days) 5-30 N	%	31-60 N	%	61-92 N	%
Probable Viral	11	47.8	30	61.2	35	58.3
Proven Viral	0	0	3	6.1	1	1.7
Total Viral	11	47.8	33	67.3	36	60.0
Probable Bacterial	6	26.1	7	14.3	16	26.7
Proven Bacterial	4	17.4	2	4.1	4	6.7
Total Bacterial	10*	43.5	9*	18.4	20	33.3
Other Infectious	0	0	1	2.0	0	0
Non-Infectious	2	8.7	6	12.2	3	5.0
Unknown	0	0	0	0	1	1.7
Total Other	2	8.7	7	14.3	4	6.7
Total Patient-Visits	23		49		60	

* $X^2 = 3.87$; $p<0.05$

Table 9. Distribution of Chief Complaints

Chief Complaint	No. of Patient-Visits	Percent of Total
Fever	67	35.8
Fever + Respiratory Symptoms	28	15.0
Respiratory Symptoms	21	11.2
Fever + Gastrointestinal Symptoms	20	10.7
Gastrointestinal Symptoms	13	7.0
Systemic Symptoms	6	3.2
Fever + Systemic Symptoms	3	1.6
Other *	25	13.4
Unspecified	4	2.1
	187	100.0

* Other: Skin rash or swelling (4); referrals from neighborhood health centers for possible admission (4); eye drainage or swelling (3); trauma (3); follow-up visit for a prior complaint (3); breast swelling (2); gastrointestinal + respiratory symptoms +/- fever (2); joint swelling (1); systemic + gastrointestinal symptoms (1); well child care (1); respiratory, systemic, and genitourinary symptoms (1)

Table 10. Distribution of Predominant Symptoms At Presentation

Symptoms	No. of Patient-Visits	% of Total
Respiratory	64	34.2
Gastrointestinal	26	13.9
Systemic	25	13.4
Gastrointestinal + Respiratory	13	7.0
Gastrointestinal + Systemic	12	6.4
Gastrointestinal + Respiratory + Systemic	12	6.4
Respiratory + Systemic	10	5.3
Other *	25	13.4
	187	100.0

*Other: None (9); rash or other skin lesion, +/- other symptoms (7); skin or joint swelling (2); breast swelling (2); eye swelling or drainage, +/- other symptoms (3); ear pulling +respiratory + gastrointestinal symptoms (1)

Table 11. The Relationship of Predominant Symptoms to Temperature

	Temperature (°F) < 100.0		≥ 100.0	
	N	%	N	%
Respiratory	25	47.2	38	28.8
Gastrointestinal	10	18.9	16	12.1
Systemic	2	3.8	22	16.7
Gastrointestinal + Respiratory	3	5.7	10	7.6
Gastrointestinal + Systemic	2	3.8	10	7.6
Gastrointestinal + Respiratory + Syst.	2	3.8	10	7.6
Respiratory + Systemic	0	0	10	7.6
Other	9	17.0	16	12.1
	53	100.0	132	100.0

Table 12. Distribution of Perinatal Complications

Complication	No. of Patient-Visits	% of Total
Prematurity/Low Birth Weight	21	11.2
Premature Rupture of Membranes	4	2.1
Maternal Fever	3	1.6
Other *	6	3.2
None	143	76.5
Not specified	10	5.3
	187	100.0

* Other: Hyperbilirubinemia requiring phototherapy (3); hypovolemia requiring transfusion (1); neonatal narcotic withdrawal(1); pustule on scalp requiring antibiotic therapy (1)

Table 13. The Relationship of Perinatal Complications to Seriousness of Illness in Febrile Infants

Final Diagnosis	Complications * N	%	No Complications N	%
Group 1	5	31.3	57	53.8
Group 2	8	50.0	35	33.0
Group 3	3	18.8	14	13.2
	16	100.0	106	100.0

* Prematurity/low birth weight, premature rupture of membranes, or maternal fever

Table 14. The Relationship of Altered Mental Status to Seriousness of Illness in Febrile Infants

I. Infants with $100 \leq T < 101$ ($^{\circ}F$)

	Mental Status			
	Irritable/Lethargic		Alert	
Final Diagnosis	N	%	N	%
Group 1	5	41.7	24	70.6
Group 2	6	50.0	9	26.5
Group 3	1	8.3	1	2.9
Total	12+	100.0	34	100.0

II. Infants with $101 \leq T < 102$ ($^{\circ}F$)

Final Diagnosis				
Group 1	2 *	12.5	10 *	58.8
Group 2	7	43.8	3	17.6
Group 3	7	43.8	4	23.5
Total	16+#	100.0	17	100.0

III. Infants with $T \geq 102$ ($^{\circ}F$)

Final Diagnosis				
Group 1	7	33.3	2	33.3
Group 2	9	42.9	1	16.7
Group 3	5	23.8	3	50.0
Total	21#	100.0	6	

* $p = 0.0065$; Fisher's exact

\+ $\chi^2 = 12.24$; $p < 0.001$

\# $\chi^2 = 8.90$; $p < 0.01$

Table 15. The Relationship of WBC Count to Seriousness of Illness in Febrile Infants

Final Diagnosis	WBC Count (X 1000) 4.0-9.9 N	%	10.0-14.9 N	%	15.0-31.3 N	%
Group 1						
URI	6		2		3	
Fever No Source	6		2		5	
Well Baby	0		0		0	
Mastitis	1		1		0	
Skin/Wound Infection	1		0		0	
Conjunctivitis	0		1		0	
Other	2		0		0	
Total Group 1	16	50.0	6	18.2	8	32.0
Group 2						
Otitis Media	6		7		6	
Gastroenteritis	4		2		2	
Bronchiolitis	1		7		0	
Croup	1		0		0	
Varicella	1		0		0	
Total Group 2	13	40.6	16	48.4	8	32.0
Group 3						
Pneumonia	1		8		1	
Meningitis	2		1		2	
Bacteremia	0		2		1	
UTI	0		0		3	
Septic Arthritis/Osteo	0		0		2	
Total Group 3	3	9.4	11	33.3	9	36.0
Total N	32		33		25	

Table 16. The Relationship of WBC Count to Microbiologic Diagnosis in Febrile Infants

	WBC Count (X 1000) 4.0-9.9		10.0-14.9		15.0-31.3	
	N	%	N	%	N	%
Proven Bacterial	3	9.4	2	6.1	5	21.7
Probable Bacterial	7	21.9	11	33.3	7	30.4
Total Bacterial	10	31.3	13	39.4	12	52.2
Proven Viral	0	0	4	12.1	0	0
Probable Viral	20	62.5	16	48.5	11	47.8
Total Viral	20	62.5	20	60.6	11	47.8
Other Infectious	0	0	0	0	0	0
Non-Infectious	1	3.1	0	0	0	0
Unknown	1	3.1	0	0	0	0
Total Other	2	6.3	0	0	0	0
Total N	32	100.0	33	100.0	23	100.0

Table 17. The Relationship of Percent PMNs to Seriousness of Illness in Febrile Infants

Final Diagnosis	Percent PMNs 6-24 N	%	25-49 N	%	50-74 N	%
Group 1						
URI	6		3		2	
Fever No Source	3		8		2	
Well Baby	0		0		0	
Mastitis	0		2		0	
Skin/Wound Infection	0		1		0	
Conjunctivitis	0		1		0	
Other	1		1		0	
Total Group 1	10	41.7	16	32.0	4	25.0
Group 2						
Otitis Media	4		12		3	
Gastroenteritis	2		4		2	
Bronchiolitis	4		4		0	
Croup	0		1		0	
Varicella	1		0		0	
Total Group 2	11	45.8	21	42.0	5	31.3
Group 3						
Pneumonia	3		6		1	
Meningitis	0		5		0	
Bacteremia	0		1		2	
UTI	0		1		2	
Septic Arthritis/Osteo	0		0		2	
Total Group 3	3	12.5	13	26.0	7	43.8
Total N	24	100.0	50	100.0	16	100.0

Table 18. The Relationship of Percent PMNs to Microbiologic Diagnosis in Febrile Infants

	Percent PMNs 6-24		25-49		50-74	
	N	%	N	%	N	%
Proven Bacterial	1	4.2	5	10.0	4	25.0
Probable Bacterial	5	20.8	16	32.0	6	37.5
Total Bacterial	6	25.0	21	42.0	10	62.5
Proven Viral	3	12.5	1	2.0	0	0
Probable Viral	14	58.3	27	54.0	6	37.5
Total Viral	17	70.8	28	56.0	6	37.5
Other Infectious	0	0	0	0	0	0
Non Infectious	1	4.2	0	0	0	0
Unknown	0	0	1	2.0	0	0
Total Other	1	4.2	1	2.0	0	0
Total N	24	100.0	50	100.0	16	100.0

Table 19. The Relationship of Absolute PMNs to Seriousness of Illness in Febrile Infants

Final Diagnosis	PMNs/mm^3 < 5000 N	%	5000-9999 N	%	≥10,000 N	%
Group 1						
URI	10		1		0	
Fever No Source	8		3		2	
Well Baby	0		0		0	
Mastitis	1		1		0	
Skin/Wound Infection	1		0		0	
Conjunctivitis	1		0		0	
Other	2		0		0	
Total Group 1	23	39.0	5	20.0	2	33.3
Group 2						
Otitis Media	11		7		1	
Gastroenteritis	5		3		0	
Bronchiolitis	8		0		0	
Croup	1		0		0	
Varicella	1		0		0	
Total Group 2	26	44.0	10	40.0	1	16.7
Group 3						
Pneumonia	8		2		0	
Meningitis	2		3		0	
Bacteremia	0		2		1	
UTI	0		3		0	
Septic Arthritis/Osteo	0		0		2	
Total Group 3	10	16.9	10	40.0	3	50.0
Total N	59	100.0	25	100.0	6	100.0

Table 20. The Relationship of Absolute PMNs to Microbiologic Diagnosis in Febrile Infants

	PMNs/mm^3					
	<5000		5000-9999		≥10,000	
	N	%	N	%	N	%
Proven Bacterial	3	5.1	6	24.0	1	16.7
Probable Bacterial	15	25.4	9	36.0	3	50.0
Total Bacterial	18	30.5	15	60.0	4	66.7
Proven Viral	4	6.8	0	0	0	0
Probable Viral	35	59.3	10	40.0	2	33.3
Total Viral	39	66.1	10	40.0	2	33.3
Other Infectious	0	0	0	0	0	0
Non Infectious	1	1.7	0	0	0	0
Unknown	1	1.7	0	0	0	0
Total Other	2	3.4	0	0	0	0
Total N	59	100.0	25	100.0	6	100.0

Table 21. The Relationship of Percent Bands to Seriousness of of Illness in Febrile Infants

Final Diagnosis	Percent Bands 0-5 N	%	6-34 N	%
Group 1				
URI	9		2	
Fever No Source	10		3	
Well Baby	0		0	
Mastitis	1		1	
Skin/Wound Infection	1		0	
Conjunctivitis	0		1	
Other	0		2	
Total Group 1	21	32.3	9	36.0
Group 2				
Otitis Media	16		3	
Gastroenteritis	3		5	
Bronchiolitis	7		1	
Croup	1		0	
Varicella	1		0	
Total Group 2	28	43.1	9	36.0
Group 3				
Pneumonia	7		3	
Meningitis	4		1	
Bacteremia	1		2	
UTI	3		0	
Septic Arthritis/Osteo	1		1	
Total Group 3	16	24.6	7	28.0
Total N	65		25	

Table 22. The Relationship of Percent Bands to Microbiologic Diagnosis in Febrile Infants

	Percent Bands 0-5 N	%	6-34 N	%
Proven Bacterial	5*	7.7	5*	20.0
Probable Bacterial	21	32.3	6	24.0
Total Bacterial	26	40.0	11	44.0
Proven Viral	3	4.6	1	4.0
Probable Viral	36	55.4	11	44.0
Total Viral	39#	60.0	12#	48.0
Other Infectious	0	0	0	0
Non Infectious	0	0	1	4.0
Unknown	0	0	1	4.0
Total Other	0	0	2	8.0
Total N	65		25	

* $X^2 = 4.13$; $p < 0.05$

$X^2 = 4.78$; $p < 0.05$

Table 23. The Relationship of Absolute Band Count to Seriousness of Illness in Febrile Infants

	Bands/mm^3									
	0-249		250-499		500-999		1000-1499		≥1500	
Final Diagnosis	N	%	N	%	N	%	N	%	N	%
Group 1										
URI	7		1		2		1		0	
Fever No Source	9		0		0		2		2	
Well Baby	0		0		0		0		0	
Mastitis	0		1		1		0		0	
Skin Wound Infection	1		0		0		0		0	
Conjunctivitis	0		0		1		0		0	
Other	0		1		0		0		1	
Total Group 1	17	41.5	3	15.8	4	28.6	3	42.9	3	33.3
Group 2										
Otitis Media	8		5		4		1		1	
Gastroenteritis	1		4		1		1		1	
Bronchiolitis	5		1		2		0		0	
Croup	1		0		0		0		0	
Varicella	1		0		0		0		0	
Total Group 2	16	39.0	10	52.6	7	50.0	2	28.6	2	22.2
Group 3										
Pneumonia	2		4		1		2		1	
Meningitis	4		0		1		0		0	
Bacteremia	1		0		0		0		2	
UTI	1		1		1		0		0	
Septic Arthritis/Ost	0		1		0		0		1	
Total Group 3	8*	19.5	6	31.6	3	21.4	2	28.6	4*	44.4
Total N	41		19		14		7		9	

* $p = 0.04$; Fisher's exact test

Table 24. The Relationship of Absolute Band Count to Microbiologic Diagnosis in Febrile Infants

	Bands/mm^3									
	0-249		250-499		500-999		1000-1499		≥1500	
	N	%	N	%	N	%	N	%	N	%
Proven Bacterial	2		4		1		1		2	
Probable Bacterial	10		7		5		2		3	
Total Bacterial	12	29.3	11	57.9	6	42.9	3	42.9	5	55.6
Proven Viral	3		0		0		1		0	
Probable Viral	26		7		8		3		3	
Total Viral	29	70.7	7	36.8	8	57.1	4	57.1	3	42.9
Other Infectious	0		0		0		0		0	
Non Infectious	0		0		0		0		1	
Unknown	0		1		0		0		0	
Total Other	0	0	1	5.3	0		0	0	1	11.1
Total N	41		19		14		7		9	

Table 25. The Sensitivity and Specificity of Various WBC Parameters for Serious Illness and Bacterial Illness in Febrile Infants

	Group 3 Illness		Proven Bacterial Illness		Proven + Probable Bacterial Illness	
	Sens.	Spec.	Sens.	Spec.	Sens.	Spec.
WBC ≥ 10000	85.7 %	42.2 %	70.0 %	37.2 %	71.4 %	40.4 %
WBC ≥ 15000	50.0 %	76.6 %	50.0 %	76.6 %	34.3 %	78.4 %
% PMN ≥ 25	87.0 %	31.3 %	90.0 %	28.7 %	83.8 %	37.0 %
% PMN ≥ 50	30.4 %	88.3 %	40.0 %	84.8 %	37.0 %	88.7 %
PMN ≥ 5000	56.5 %	73.1 %	70.0 %	70.0 %	51.4 %	77.4 %
% Bands > 5	30.4 %	73.1 %	50.0 %	75.0 %	29.7 %	73.6 %
Bands ≥ 250	66.7 %	50.0 %	80.0 %	48.1 %	67.6 %	54.7 %
Bands ≥ 500	41.7 %	68.6 %	40.0 %	67.5 %	37.8 %	69.8 %

Table 26. The Relationship of WBC Count to Seriousness of Illness in Infants 5-30 Days with T ≥ 100°F

Final Diagnosis	WBC < 10,000/mm^3	WBC ≥ 10,000/mm^3
Group 1		
URI	1	0
Fever No Source	2	2
Well Baby	0	0
Mastitis	1	0
Skin/Wound Infection	0	0
Conjunctivitis	0	0
Other	0	0
Total Group 1	4	2
Group 2		
Otitis Media	1	0
Gastroenteritis	0	1
Bronchiolitis	0	0
Croup	0	0
Varicella	1	0
Total Group 2	2	1
Group 3		
Pneumonia	0	2
Meningitis	0	1
Bacteremia	0	2
UTI	0	0
Septic Arthritis/Osteo	0	2
Total Group 3	0	7
Total N	6	10

Table 27. The Relationship of WBC Count to Seriousness of Illness in Infants 31-92 Days with T $\geq$ 101° F

Final Diagnosis	WBC < 10,000/mm^3	WBC $\geq$ 10,000/mm^3
Group 1		
URI	2	2
Fever No Source	3	5
Well Baby	0	0
Mastitis	0	0
Skin/Wound Infection	0	0
Conjunctivitis	0	1
Other	1	0
Total Group 1	5	8
Group 2		
Otitis Media	2	8
Gastroenteritis	3	3
Bronchiolitis	0	4
Croup	0	0
Varicella	0	0
Total Group 2	5	15
Group 3		
Pneumonia	1	6
Meningitis	2	2
Bacteremia	0	1
UTI	0	3
Septic Arthritis/Osteo	0	0
Total Group 3	3	12
Total N	13	35

FIGURE 1 Record Form

FEVER IN INFANTS LESS THAN THREE MONTHS

RECORD FORM

Name _____

Hospital Number (unknown = 999-99-99) _ _ _-_ _-_ _ _ (1-7)

Study Number _ _ _ _ (8-12)

Date of Birth _ _/_ _/_ _ (13-18)
mo day yr

Date of Visit _ _/_ _/_ _ (19-24)
mo day yr

Age in days _ _ (25-26)

Sex 1=male 2=female 9=unspecified _ (27)

Racial/Ethnic Origin 1=white 2=black 3=oriental 4=hispanic
5=other _____ 9=unspecified _ (28)

HISTORICAL DATA

Chief Complaint _____
1=Fever(include "felt warm") 4=Systemic _ (29)
2=GI 5=Other
3=Respiratory 9=Unspecified

Temperature at home (999.9=unspecified or unknown) _ _ _._ (30-33)

Symptoms at Presentation _ (34)
1=GI
__vomiting __abdominal pain
__diarrhea __other_____
__constipation

2=Respiratory
__coughing __tachypnea
__rhinorrhea __cyanosis
__sneezing __congestion
__"trouble breathing" __other_____

3=Systemic
__anorexia __seizure
__lethargy __comatose
__irritable/fussy __other_____

4=Other_____
5=GI + Respiratory
6=GI + Systemic
7=Respiratory + Systemic
8=GI + Respiratory + Systemic
9=Unspecified

Illness in Family Member
1=None 4=Systemic _ (35)
2=GI 5=Other_____
3=Respiratory 9=Unspecified
Describe_____

Perinatal Complications _ (36)
1=None
2=BW<2500 g or GA<37 wks BW _____
3=maternal fever GA _____
4=PROM
5=any combination 2+3, 3+4, 2+4
6=2+3+4
7=Other_____
9=Unspecified

Risk Factors for Infection (e.g. VP Shunt, etc.) _ (37)
1=No
2=Yes. Describe_____
9=Unspecified

Prior Antibiotic Rx (within two days of visit) _ (38)
1=None 5=Erythromycin-Sulfa
2=Amoxicillin or Ampicillin 6=Cefaclor
3=Trimethoprim-Sulfa 7=PCN V
4=Erythromycin 8=Other_____
9=not specified

PHYSICAL EXAMINATION

Temperature at PWI 999.9=not taken or not specified _ _ _._ (39-42)

Toxicity 1=Toxic 2=Non-toxic 9=Not Specified _ (43)

Consolability 1=Consolable 2=Not Consolable 9=Unspecified _ (44)

Level of Consciousness _ (45)
1=Alert 4=Comatose
2=Irritable/Fussy 5=Seizing
3=Lethargic 9=Not Specified

LABORATORY DATA

Total WBC (X 1000) (99.9=Not done) _ _._ (46-48)

Differential
%Polys (999=Not done) _ _ _ (49-51)
%Bands (99=Not done) _ _ (52-53)
__Monos __Lymphs __Eos __Baso __Atyp

Platelets (X 1000) (999=Not done) _ _ _ (54-56)

Urinalysis 1=normal 4=abnormal dipstick + _ (57)
2=abnormal dipstick microscopic
3=abnormal microscopic 5=not done
9=not specified

ESR
(999=not specified) _ _ _ (58-60)

CXR
1=no infiltrate 4=not done _ (61)
2=infiltrate 9=not specified
3=equivocal

Lumbar Puncture 1=not done 4=done abnormal _ (62)
2=done and normal 5=equivocal
3=traumatic 9=not specified
color_____ O.P._____
protein_____ C.S.F./serum glucose_____
WBC_____ Diff: _____polys _____lymphs _____monos
RBC_____ Gram stain_____

Blood Cultures 1=negative 11=Klebsiella _ _ (63-64)
2=Group B Strep 12=Meningococcus
3=S. pneumoniae 13=Proteus
4=H. influenzae 14=Pseudomonas
5=E. coli 15=Strep pyogenes
6=Salmonella 16=other gm -_____
7=Staph aureus 17=other gm +_____
8=Group D Strep 18=not done
9=Strep viridans 99=not specified
10=Staph epidermidis
Bottles positive _____TSB _____BHI

CSF Cultures _ _ (65-66)

Urine Cultures _____Colony Ct _____ No. positive cultures _ _ (67-68)

MEF Cultures _ _ (69-70)

Stool Cultures 1=Not done 5=Enteropathogenic E. coli _ (71)
2=Salmonella 6=Negative/Nl flora
3=Yersinia 7=Shigella
4=Campylobacter 9=Not specified

Skin/Wound Cultures _ (72)
1=negative 4=Other_____
2=Staph aureus 5=Nl. flora_____
3=Strep pyogenes 6=Not done
9=Not specified

PWI Diagnosis 1=fever no source 13=r/o sepsis _ _ (73-74)
2=otitis media 14=r/o meningitis
3=URI 15=septic arthritis/osteo
4=pneumonia 16=peritonitis
5=UTI/pyelo 17=conjunctivitis
6=skin/wound infection 18=omphalitis
7=meningitis 19=mastitis
8=bacteremia 20=bronchiolitis
9=febrile seizure 21=croup
10=pharyngitis 22=other_____
11=gastroenteritis 99=not specified
12=dehydration

Final Diagnosis _ _ (75-76)

Microbiologic Diagnosis _ (77)
1=proven bacterial 5=other infectious_____
2=probable bacterial 6=non-infectious
3=probable viral 9=unknown
4=proven viral

Disposition 1=home 2=hospital 9=unspecified _ (78)

Therapy _ (79)
1=None
2=IM or IV amp and gent for 72 h or less
3=IM or IV amp and gent for >72 h
4=IV or IM ampicillin
5=IV amp and chloro
6=po amoxicilin/ampicillin
7=trimethoprim-sulfa
8=other_____
9=not specified

Outcome _ (80)
1=uneventful home
2=uneventful hospital
3=complicated home_____
4=complicated hospital_____
5=other_____
9=not specified

Clinical Notes:

FIGURE 2 Distribution of Patient-Visits by Temperature and Age

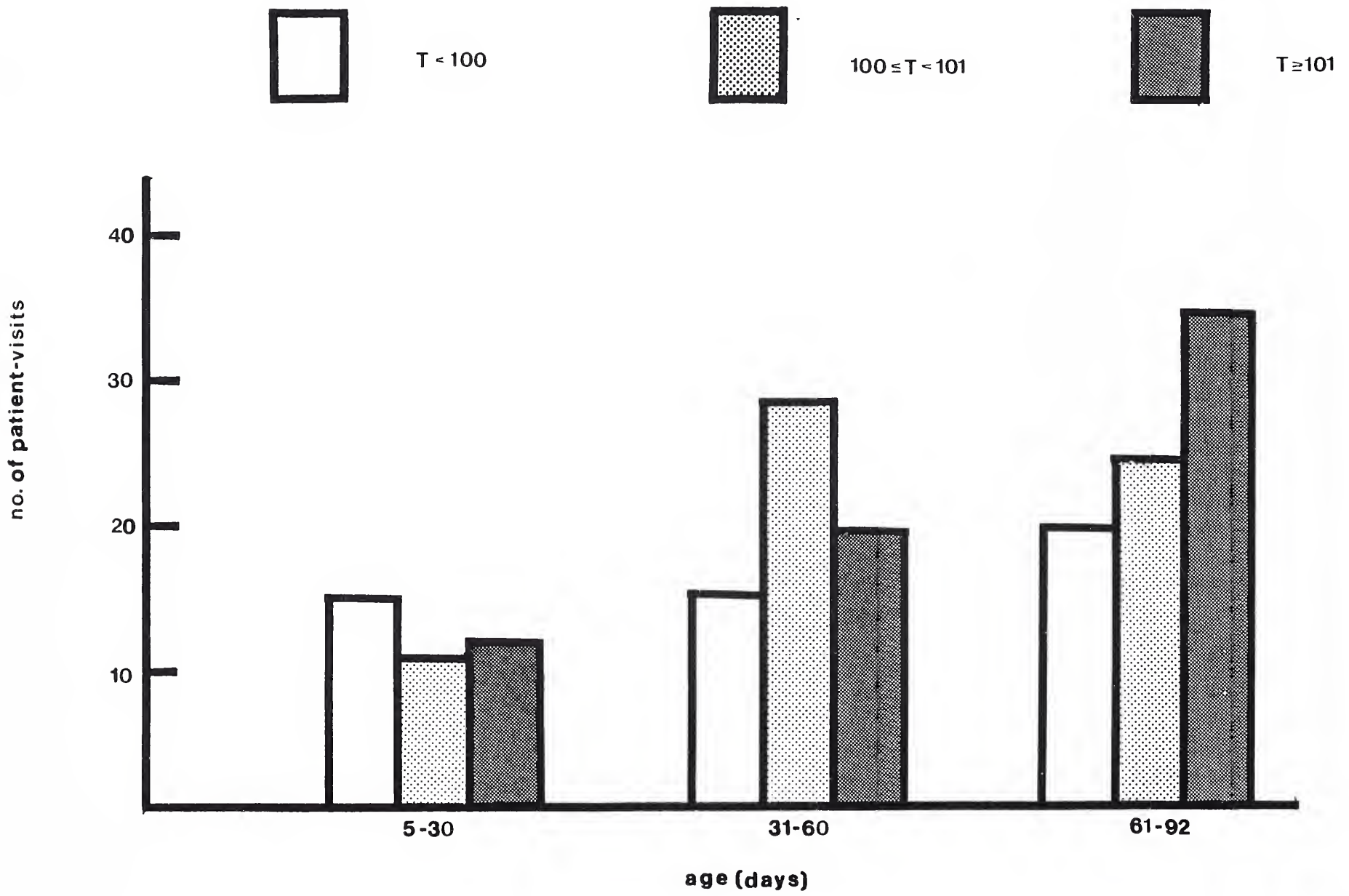


FIGURE 3 Temperature at Home Vs. in PWIC

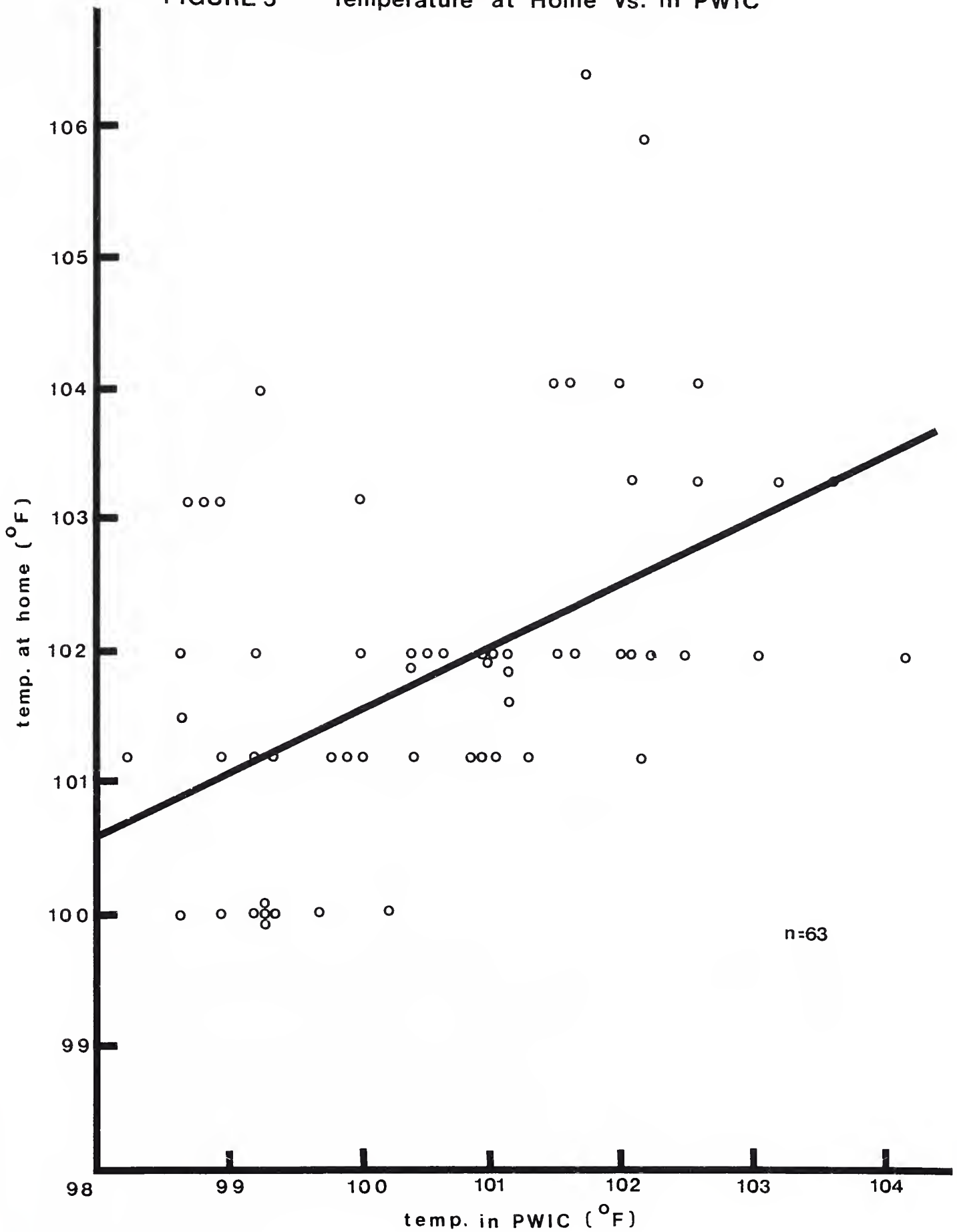


FIGURE 4 Seriousness of Illness Vs. Temperature

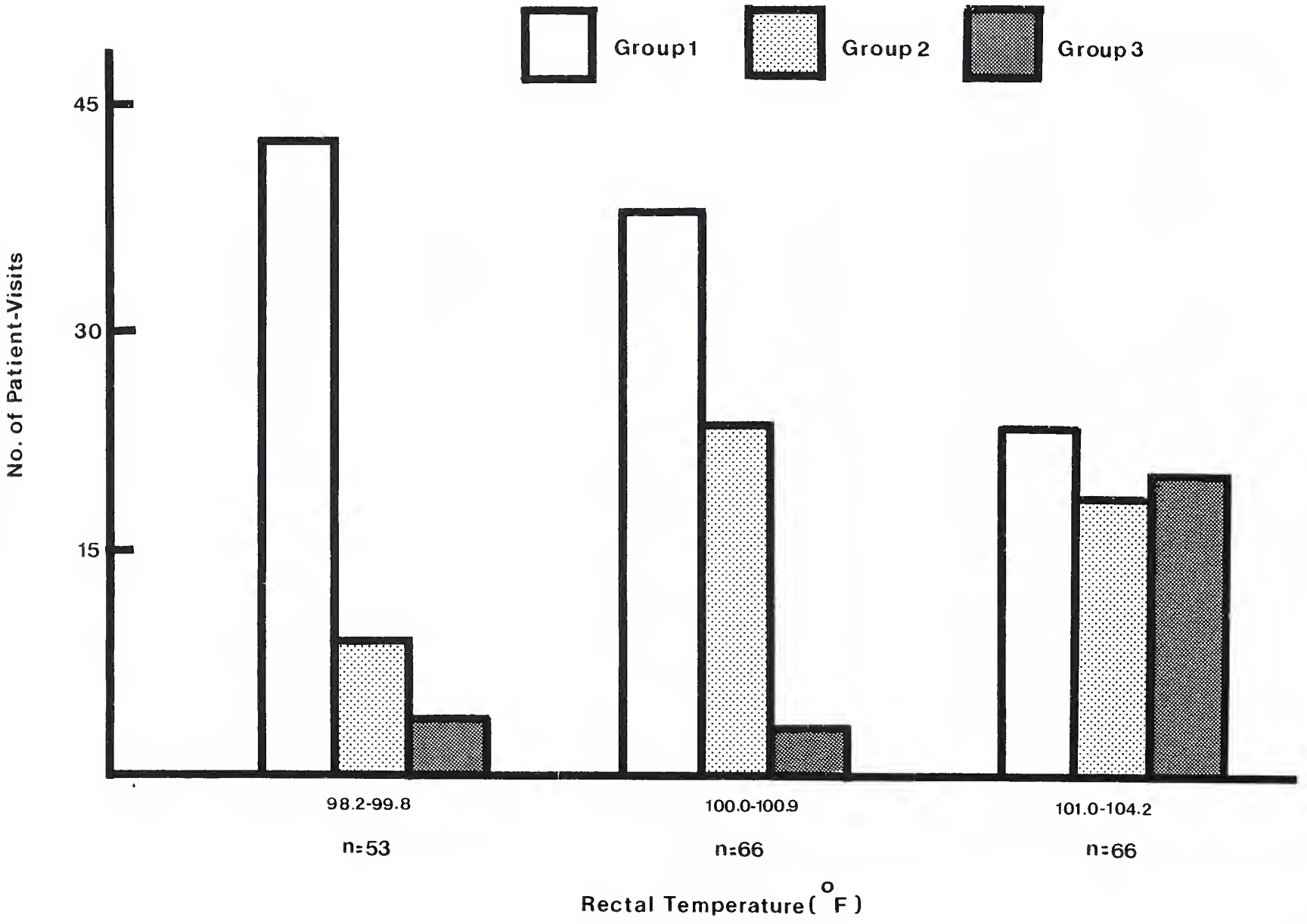


FIGURE 5 Microbiologic Diagnosis Vs. Temperature

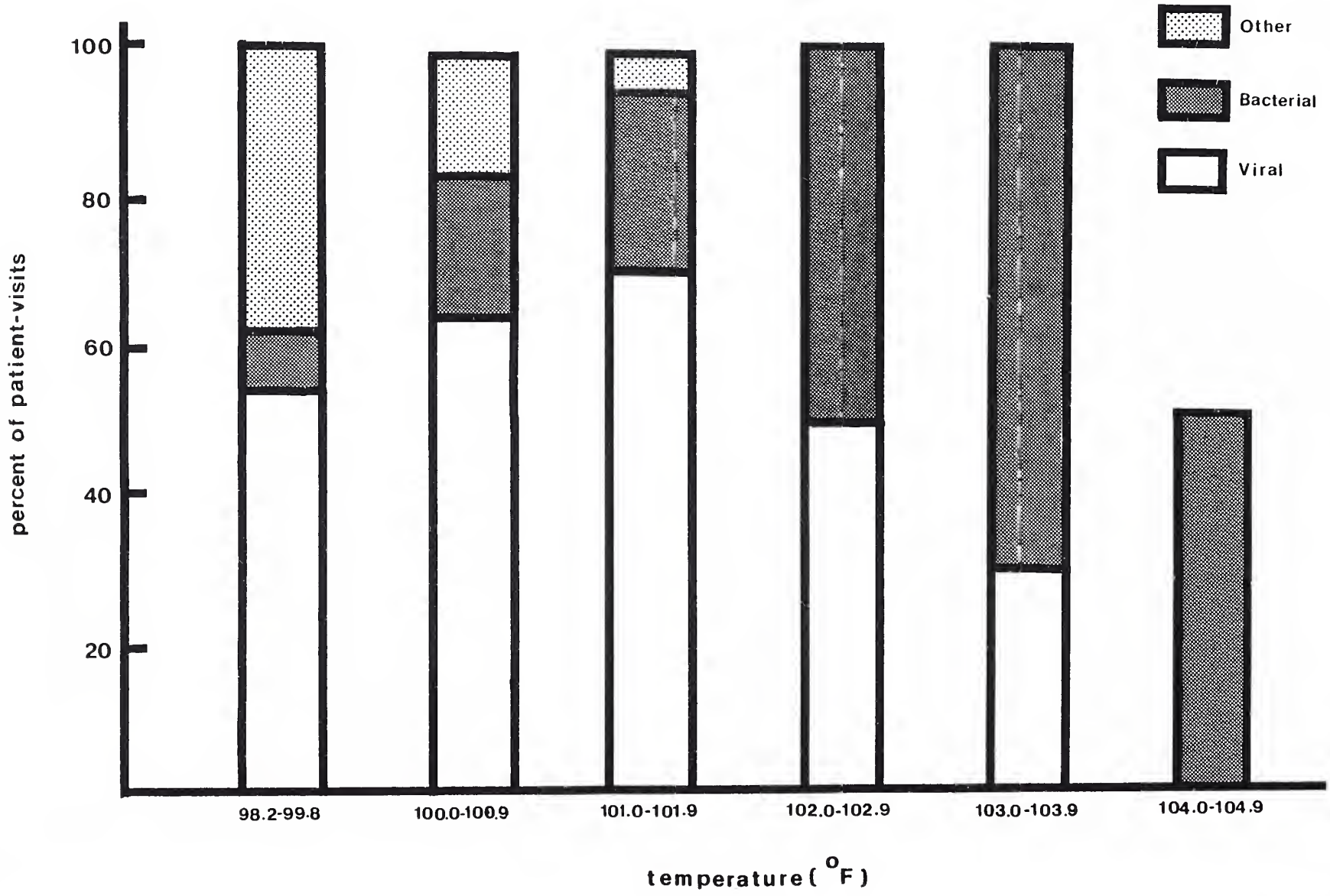
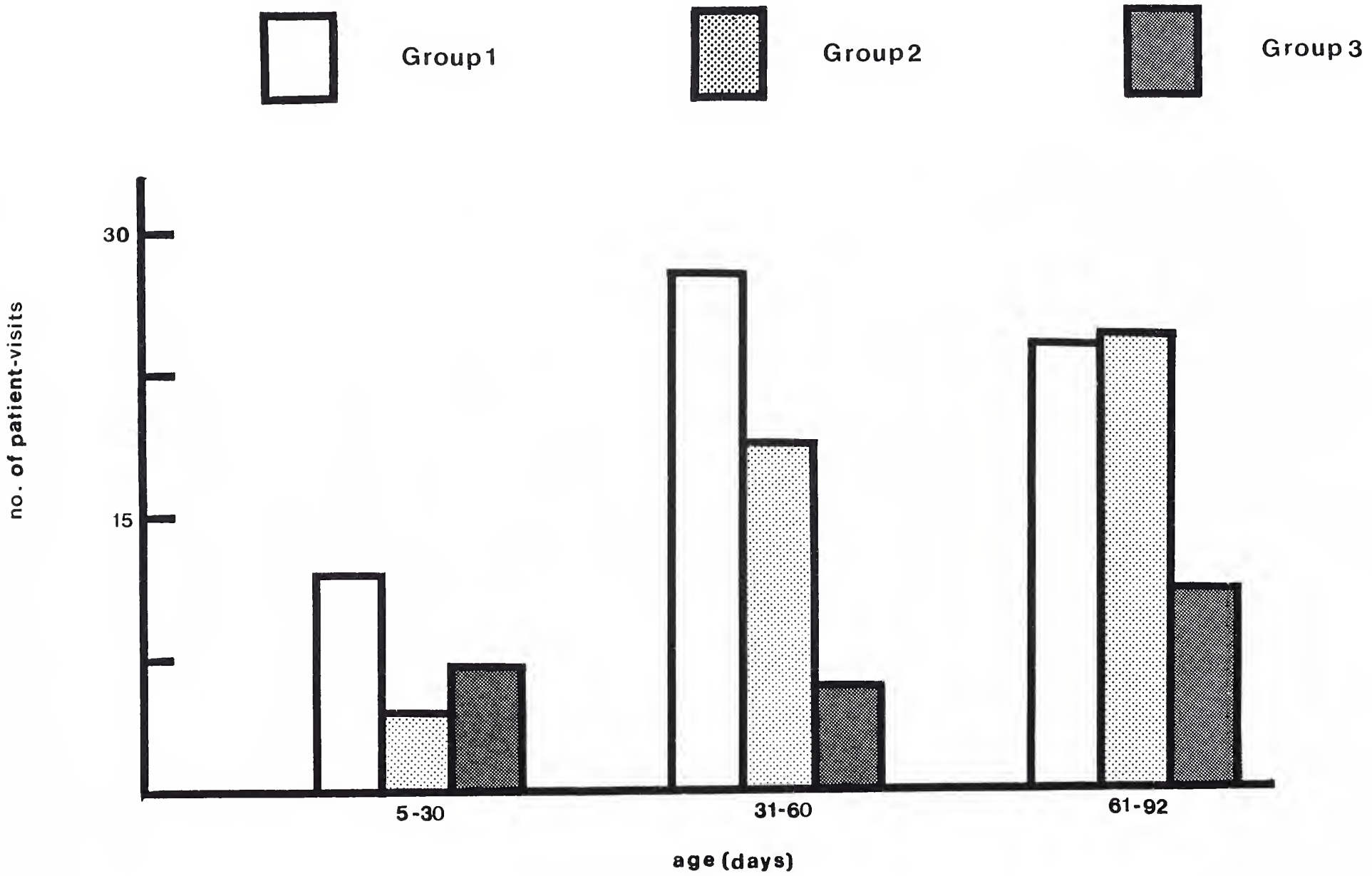


FIGURE 6

Seriousness of Illness Vs. Age



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